REMARKS

In the outstanding Office action, claims 1 to 13 and 15 to 25 were presented for examination. Claims 11, 12, 15, and 17 stand withdrawn from further consideration. Claims 1-10, 13, 16 and 18-25 were rejected.

In this amendment applicant has cancelled claims 13, 16 and 23-25. New claim 26 has been added. Thus, claims 1-10, 13, 18-22 and 26 are now pending for examination, as will be discussed in detail below. Accordingly, it is believed that the application is in condition for allowance.

Rejoinder

Applicant notes that claims 11, 12, 15 and 17 stand withdrawn from further consideration.

Objections and Rejections Withdrawn

Applicant appreciates the withdrawal of the objections and rejections made in the prior Office action. The rejections now made in the current Office action are addressed herein.

Claim Amendments

Claims 13, 16 and 23 to 25 have been canceled to reduce the issues.

Claim 1 has been amended to relate to a method of preventing crystallization of recombinant or synthetic gelatin in a vaccine composition. Support for this amendment can be found at page 13, lines 11-17 of applicant's specification.

New claim 26 depends from claim 1 and recites that the water content of the vaccine composition is reduced to be between 1 weight percent and 2 weight percent. Support for new claim 26 can be found at page 8, lines 21-22 of applicant's specification.

Claim Rejections - 35 U.S.C. § 103, Alleged Unpatentability

In the outstanding Office action, claims 1-10, 13, 16 and 18 to 25 were rejected under 35 U.S.C. § 103 as allegedly being unpatentable over WO 01/34801 et al. ("the '801 publication" herein), in view of Applied Microbiology volume 20, pages 935-938 (1970) to Greiff.

The Office action describes the '801 publication as teaching a method of producing a lyophilized vaccine formulation comprising a recombinant gelatin having certain features which vaccine formulation is alleged to be pertinent to certain ones of applicant's claims, as set forth in the Office action.

In addition, the Office action acknowledges that the '801 publication does not teach reducing and maintaining the water content to be below 2 weight percent as is recited in applicant's claim 1.

However, the Office action also refers to Greiff as teaching the lyophilization of influenza virus and that a moisture content of 1.6% ("e.g. below 2%") after lyophilization is found best for stabilization of the vaccine composition.

Based on these disclosures, the Office action concludes that it would have been obvious to one of ordinary skill in the art to reduce the water content to "1.6% as taught by Greiff" in the method of making a vaccine comprising a gelatin as taught by the '801 publication

In reply, Applicant respectfully submits that the invention claimed in amended claim 1 is unobvious, and therefore patentable, over any combination of Greiff with the '801 publication because a person of ordinary skill in the art would not have been motivated to employ Greiff's reduced water content of 1.6% in the '801 publication's

vaccine composition, for the purposes of the invention claimed in claim 1, and would have been uncertain of success, the reasons for which will now be explained.

The invention claimed in amended claim 1 solves a problem, namely, the problem of crystallization which can occur in vaccine compositions comprising recombinant or synthetic gelatin as a stabilizer. This problem is described at page 7, line 19 to page 8, line 15, of applicant's specification but does not appear to have been described in the '801 publication or in any other art, prior to the claimed invention.

The claimed invention solves the problem of crystallization occurring in a vaccine composition employing a recombinant or synthetic gelatin by reducing the water content of the vaccine composition to be below 2 weight percent and maintaining the water content below 2 weight percent for at least 2 years.

Greiff appears to teach that a residual moisture content of 1.6% provides maximum stability in some of his influenza virus preparations but Greiff does not appear to provide an unambiguous teaching that reducing and maintaining the water content below 2 weight percent will improve the stability of influenza virus preparations or other vaccine compositions. To the contrary, Greiff describes and shows that some other influenza virus preparations have maximum stability at a higher residual moisture content of 2.8%. Thus, Greiff's teaching does not appear to suggest that reducing the water content below 2 weight percent will necessarily increase the stability of a vaccine composition.

Therefore, Greiff's teaching apparently would not give a person of ordinary skill in the art a reasonable expectation that reducing and maintaining the water content below 2 weight percent would succeed in stabilizing a vaccine composition comprising a recombinant or synthetic gelatin. Rather, Greiff appears to teach a skilled person that a residual moisture content of 1.6% would be effective in some circumstances, and 2.8%

would be effective in others, for stabilizing his particular influenza virus preparation, leaving uncertainty as to the efficacy of reducing and maintaining the water content below 2 weight percent in a vaccine composition comprising a recombinant or synthetic gelatin.

The role of gelatin (recombinant or synthetic gelatin in amended claim 1) introduces another factor into the relationship between stability and moisture content, which factor was not considered by Greiff. The presence of recombinant or synthetic gelatin in the vaccine compositions described in the '801 publication appears to adding to the uncertainty of the outcome obtainable in attempting to apply the teachings of Greiff to the vaccine composition described in the '801 publication.

Therefore, applicant believes a person of ordinary skill in the art would not have a reasonable expectation of success in attempting to combine the teachings of Greiff with those of the '801 publication for the purposes of applicant's claimed invention.

Moreover, at the date of applicant's invention a skilled person apparently would not have been motivated to employ Greiff's teaching in an attempt to solve the problem of recrystallization occurring in a vaccine composition comprising a recombinant or synthetic gelatin, because Greiff's teaching does not take account of the stabilizing role of gelatin.

Considering Greiff in more detail, Greiff discloses that influenza virus preparations having a residual moisture content of 1.6%, and sealed under helium or argon, were more stable than preparations having a higher residual moisture content of 2.8%. However, Greiff also describes that similar influenza virus preparations sealed under nitrogen or oxygen were less stable than preparations having a residual moisture content of 2.8%. Thus, the content of residual moisture for maximum stability of the influenza virus preparation varies with the gas under which the dried product is sealed,

according to Greiff. (See the abstract, Table 3 and the Discussion in Greiff.) Also, overdrying, for example to a moisture content of 0.6% can reduce stability.

As is discussed in applicant's specification, prior to the claimed invention, vaccine stability was known to be influenced by a number of factors including moisture, the constituents of the vaccine, and the surrounding gas. One or more of a variety of stabilizers was generally used to improve vaccine stability. (See page 2, lines 4-8 of applicant's specification.)

Gelatin and gelatin derivatives such as hydrolyzed or partially hydrolyzed gelatin were successfully used as stabilizers in a number of vaccine compositions prior to the claimed invention. At page 2, lines 13-31, applicant's specification describes a number of successful uses of gelatin or gelatin derivatives to stabilize vaccines, citing seven patent publications in support.

Greiff does not employ gelatin or gelatin derivatives in the influenza virus preparations he describes and does not discuss the role of gelatin in stabilizing vaccines. Because Greiff was published in 1970, before most, if not all of the previously noted patent publications, a skilled person might reasonably believe that the varying stability problems described by Greiff were problems that could be solved by the use of gelatin or a gelatin derivative as a stabilizer, as is described in the aforesaid patent publications published subsequently to Greiff.

Greiff correlates the water content to the stability of the influenza virus particles he studied referring to water bound to protein coat carboxy and amino groups and to "random water" present on the protein surface. (See Greiff's Discussion, lefthand column.) A skilled person could reasonably consider such water content considerations to be less significant when a gelatin stabilizer is present in the vaccine composition to act as a protective colloid. As explained at page 3, line 31 to page 4, line 2 of applicant's

specification, when using animal-derived gelatins, which are usually heterogeneous in nature, crystallization problems were not observed.

That vaccine compositions comprising recombinant gelatins have a tendency to crystallize, adversely impacting the effectiveness of the vaccine, was not known until the inventors of the present application discovered the phenomenon when making a lyophilized vaccine composition comprising recombinant gelatin instead of animal-derived gelatin. (See page 7, lines 19-25 of applicant's specification.)

The crystallization problem solved by the claimed invention is specific to vaccine compositions employing recombinant or synthetic gelatin as a stabilizer and to applicant's knowledge does not occur with analogous compositions comprising animal-derived gelatin. (See page 3, lines 28-30 of applicant's specification.)

Therefore, because Greiff, being published in 1970 was published before recombinant gelatin or synthetic gelatin were known, and because the instability problems described in Greiff could apparently be overcome by using gelatin, a skilled person apparently would not be motivated to attempt to combine Greiff's teaching with the vaccine composition described in the '801 publication. Moreover, following Greiff's teaching, the skilled person apparently would be uncertain of success, as has already been explained herein.

Accordingly, for all the foregoing reasons, applicant respectfully submits that amended claim 1 is unobvious and therefore patentable and allowable. Early and favorable reconsideration, and allowance, are respectfully requested.

Dependent Claims

Claims 1-10, 13, 18-22 and 26 depend either directly or indirectly from amended claim 1, incorporate all the limitations of claim 1 and therefore appear to be allowable

for at least the same reasons that amended claim 1 appears to be allowable. Applicant believes that dependent claims 1-10, 13, 18-22 and 26 also are patentably distinguishable from the art of record, and therefore allowable, by the additional limitations they recite.

Conclusion

In view of the above amendments and the discussion relating thereto, it is respectfully submitted that the instant application, as amended, is in condition for allowance. Favorable reconsideration and allowance are earnestly solicited. If for any reason the Examiner feels that consultation with applicant's representative would be helpful in the advancement of the prosecution, the Examiner is invited to contact the undersigned practitioner.

Respectfully submitted,

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